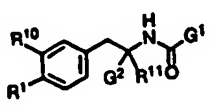
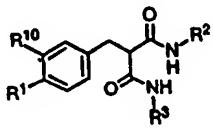




## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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|--|-----------|---|
| <b>(51) International Patent Classification <sup>6</sup>:</b><br>C07C 237/22, 237/20, 235/78, 305/24,<br>C07D 257/04, 207/20, A61K 31/165,<br>31/195, 31/41, 31/40, C07K 5/06  | <b>A3</b> | <b>(11) International Publication Number:</b> <b>WO 99/11606</b><br><br><b>(43) International Publication Date:</b> 11 March 1999 (11.03.99)  |
| <b>(21) International Application Number:</b> PCT/US98/17327<br><br><b>(22) International Filing Date:</b> 24 August 1998 (24.08.98)<br><br><b>(30) Priority Data:</b><br>680057,730 28 August 1997 (28.08.97) US<br><br><b>(71) Applicant (for all designated States except US):</b> PHARMACIA<br>& UPJOHN COMPANY [US/US]; 301 Henrietta Street,<br>Kalamazoo, MI 49001 (US).<br><br><b>(72) Inventor; and</b><br><b>(75) Inventor/Applicants (for US only):</b> LARSEN, Scott, D.<br>[US/US]; 56 Naples Court, Kalamazoo, MI 49009 (US).<br>MAY, Paul, D. [US/US]; 7890 North 32nd Street, Richland,<br>MI 48883 (US). BLEASDALE, John [GB/US]; 3230 Lites<br>End Court, Portage, MI 49024 (US). LILJEBRIS, Charlotta<br>[SE/SE]; Herrhagens byväg 63, S-752 67 Uppsala (SE).<br>SCHOSTARITZ, Heinrich, Josef [US/US]; 3236 Lost Pine<br>Way, Portage, MI 49024 (US). BARF, Tjeerd [NL/SE];<br>Vikingagatan 32, S-753 34 Uppsala (SE).<br><br><b>(74) Agent:</b> WELCH, Lawrence, T.; Pharmacia & Upjohn Com-<br>pany, Intellectual Property Legal Services, 301 Henrietta<br>Street, Kalamazoo, MI 49001 (US). |           | <b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BA, BB, BG, BR,<br>BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE,<br>GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ,<br>LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,<br>MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL,<br>TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO<br>patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian<br>patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European<br>patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR,<br>IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF,<br>CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).<br><br><b>Published</b><br><i>With international search report.</i><br><i>Before the expiration of the time limit for amending the claims</i><br><i>and to be republished in the event of the receipt of amendments.</i><br><br><b>(88) Date of publication of the international search report:</b><br>8 July 1999 (08.07.99) |
| <b>(54) Title:</b> INHIBITORS OF PROTEIN TYROSINE PHOSPHATASE<br><br><div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p>(I)</p> </div> <div style="text-align: center;">  <p>(II)</p> </div> </div><br><b>(57) Abstract</b><br><br>The present invention comprises small molecular weight, non-peptidic inhibitors of formula (I) and (II) of Protein Tyrosine Phosphatase 1 (PTP1) which are useful for the treatment and/or prevention of Non-Insulin Dependent Diabetes Mellitus (NIDDM).  |           |   |

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 98/17327

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07C237/22 C07C237/20 C07C235/78 C07C305/24 C07D257/04  
 C07D207/20 A61K31/165 A61K31/195 A61K31/41 A61K31/40  
 C07K5/06

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07C A61K C07D C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No. |
|------------|--|-----------------------|
| A          | WO 96 30332 A (US HEALTH) 3 October 1996<br>cited in the application<br>see abstract; claims 1,14  | 1-4                   |
| A          | PAUL S. CHARIFSON ET AL.: "Peptide<br>ligands of pp60c-src SH2 Domains: A<br>thermodynamic and structural study"<br>BIOCHEMISTRY.,<br>vol. 36, 1997, pages 6283-6293,<br>XP002087254<br>EASTON, PA US<br>* abstract; page 6284, formula 11 * | 1-4                   |

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

8 April 1999

Date of mailing of the international search report

18.05.1999

Name and mailing address of the ISA

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Authorized officer

Rufet, J

## INTERNATIONAL SEARCH REPORT

Inter. Appl. Application No.

PCT/US 98/17327

## C (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|----------|---|-----------------------|
| X        | WO 96 33968 A (FUJI YAKUHI KOGYO KK<br>; MORIKAWA TADANORI (JP); SUDA EIKO (JP);<br>HON) 31 October 1996<br>see abstract; claim 8   | 1                     |
| P,X      | - & EP 0 832 875 A (FUJI)<br>see claim 8; examples 2C, 4A, 5B   | 1                     |
| X        | DD 151 304 A (SCHOLTYSEK PETER DIPL CHEM<br>; KAUFMANN KLAUS DIETER DR SC DI (DE);)<br>14 October 1981<br>see claim 1; example 2.7  | 1                     |
| A        | DE 23 20 387 A (BOEHRINGER MANNHEIM GMBH)<br>31 October 1974<br>see claim 1   | 1                     |
| Y        | KING F D: "BIOISOSTERES, CONFORMATIONAL<br>RESTRICTION, AND PRO-DRUGS - CASE HISTORY:<br>AN EXAMPLE OF A CONFORMATIONAL RESTRICTION<br>APPROACH"<br>1994, MEDICINAL CHEMISTRY: PRINCIPLES AND<br>PRACTICE, PAGE(S) 206 - 209, KING F D<br>XP002033086<br>see page 208 | 1,2                   |
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| A,P      | WO 98 07699 A (JAPAN TOBACCO INC ; OHRUI<br>SATOSHI (JP); SHIBATA TSUTOMU (JP); SHINK)<br>26 February 1998<br>see page 73   | 1,2                   |

# INTERNATIONAL SEARCH REPORT

Int. l. application No.  
PCT/US 98/17327

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

- 1 ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
- 2 ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
- 3 ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

The international Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

- 1 ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
- 2 ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
- 3 ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1 partly, 2 completely, 3 completely, 4 partly

Compounds according to formula (I) wherein G2 is CONHR3

2. Claims: 1 partly, 4 partly

Compounds according to formula (I) wherein G2 = H

3. Claims: 1 partly, 4 partly

Compounds according to formula (I) wherein G2 = CH2OH

4. Claims: 1 partly, 4 partly

Compounds according to claim (I) wherein G2 = CH=CHR3

5. Claims: 1 partly, 4 partly

Compounds according to formula (II)

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 98/17327

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s)   | Publication<br>date  |
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